Age and Nutritional Status by Mini-Nutritional Assessment (MNA) can discriminate Alzheimer's Disease Severity

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Abstract— *Investigate the risk factors associated with Clinical Dementia Rating (CDR) in patients with Alzheimer's disease (AD). Cross-sectional study with 43 elderly people with AD. Parameters assessing nutritional status (anthropometry and mini-nutritional assessment-MNA), neurocognitive assessment and Clinical Dementia Rating (CDR) were investigated. For the investigation of AD severity risk factors, statistical analysis was performed using logistic regression models. The level of significance adopted was 5%. No statistically significant difference in the relationship between the parameters of anthropometry nutritional assessment and the CDR score were found. In the final regression model; only MNA (p=0.0159; OR=4.815; IC95%=1.342; 17.282) and age (p=0.0481; OR= 1.097; IC95%=1.001; 1.202), were associated with the severity of the disease (CDR). Age and MNA discriminate the severity of the disease and were considered risk factors for the severity of AD.*

I. INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease prevalent in the elderly. It is well known that incorporation of lifestyle changes, as well as physical and recreational activities, diet and cognitive activity, among others, are important to prevent the disease [1]. Evidence of preventive interventions [1] could encourage or contribute to the treatment of this population. Recent studies [2,3] have indicated the importance of some nutrients which shortage is associated with the development of AD. These nutrients contribute to the synthesis of neurotransmitters, modulation in epigenetic mechanisms and with antioxidants [2.] In elderly patients with subjective cognitive decline, clinically relevant findings have been associated with the quality of the diet [3].

Regarding the nutritional status of patients with AD, a study [4] showed a high prevalence of malnutrition or risk of malnutrition detected by the mini nutritional assessment (MAN), in patients with different severity, also associated with reduced functional status. Another recent study [5] which investigated the association between nutritional status and clinical and cognitive aspects of patients with AD, showed significant progressive impairment of nutritional and cognitive indicators related to disease progression. In a cross-sectional study [6], assessing the nutritional status and body composition and mild cognitive impairment in patients with AD, the MAN score was significantly lower, compared to healthy elderly controls. Dementia was also considered an independent predictor of malnutrition risk, when compared to cognitively intact individuals [7].

Recently, a prospective multicenter study [8] investigating the nutritional status in AD and its influence on disease progression, found that nutritional impairment was highly prevalent in patients with AD. The authors also pointed out that the identification of the nutritional status in early diagnosis, could help those patients who are at a higher risk of disease progression. [8] The relevance of assessing the nutritional status with different indicators in patients with AD, was also reported in other investigations [9,10,11].

In view of all the findings discussed above, this study investigated nutritional risk factors using the clinical dementia rating (CDR), in patients with Alzheimer's disease (AD).

II.　CASES AND METHOD

This study is part of a more comprehensive research project on lifestyle aspects in elderly patients with dementia. Some nutritional aspects have been addressed in another paper [5].

This was a cross-sectional study, which included outpatient elderly individuals (n=43) aged ≥65 years with diagnosis of suspected DA, according to the Diagnostic and Statistical Manual of Mental Disorders[12], the recommendations of the European Federation of Neurological Societies[13] and the Brazilian Academy of Neurology[14]. Clinical dementia rating (CDR)[15] was used to stage the severity of dementia, that was classified as mild, moderate or severe. Patients with other serious illnesses and patients and/or caregivers unable to answer the evaluation questions were excluded. The study was approved by the institution's ethics research committee (No. 1,234,677) and was started after the guardians signed the free and informed consent form.

Methodological procedures:

a) *Nutritional assessment by anthropometry*: According to standardized procedures and cutoff points reported in the literature such as the body mass index (BMI) for the elderly[16], the calf circumference (CC)[17], the thickness of the adductor pollicis muscle (APM) [18,19], the handgrip strength (HGS) [20,21,22] and waist circumference [23,24]. The anthropometric indicators of body composition [17,25] of arm circumference (AC), triceps skinfold (TSF), arm muscle circumference (AMC) and sub-scapular skinfold (SSF), were classified in percentile distribution as: lower than the 5th percentile (<P5: depletion); between the 5th percentile and below the 10th percentile (P5¬ - <P10: risk of depletion); between 10th and 90th percentiles (P10 - P90: normal weight); above the 90th percentile and up to the 95th percentile (> P90 - P95: risk for excess) and above the 95th percentile (> P95: excess).

b) *Mini Nutritional Assessment (MNA):* The MNA questionnaire was applied and the nutritional status was classified according to the cutoff points established as eutrophic, risk of malnutrition and malnutrition [26].

c) *International physical activity questionnaire - short form (IPAQ-SF):* Physical activity was assessed according to a standardized and validated instrument for the Brazilian population [27]. For the purpose of analysis, in this study, physical activity was classified as: sedentary or active.

d) *Statistical analysis:* A descriptive analysis was performed with frequency tables for categorical variables and measures of position and dispersion for continuous variables. The Chi-square or Fisher's exact test was used, when necessary; for comparing proportions. To compare continuous or orderable measurements between 2 groups, the Mann-Whitney test was applied and among 3 groups, the Kruskal-Wallis test. Later, to identify the predictors of disease severity by the CDR clinical score, regression models were used, such as univariate and multiple logistic regression analysis. The variable selection process employed was stepwise. The level of significance adopted for the statistical tests was 5%.

III.　RESULTS

In our study's population (n=43), 16 (37.2%) patients were rated by CDR in the mild stage; 19 (44.1%) patients in the moderate stage and 8 (18.6%) patients in the severe stage. The sample included 28 (65.1%) female patients and 15 (34.9%) male patients.

There was no statistically significant difference in the relationship between all anthropometric parameters, age and IPAQ-SF with the CDR scores (Table 1).

Table 1. Descriptive analysis of the studied variables and comparisons with the CDR score.

Variables	Classification		CDR - L N=16	CDR - M N=19	CDR – G N=8	Total N=43	P-value
Age	years	x±dp	77.6 ± 6.0	82.2 ± 7.5	82.8 ± 6.3	80.6 ± 7.0	0.0959[1]
Weight	Kg	x±dp	65.8 ± 13.8	61.5 ± 13.5	55.2 ± 9.2	62.0 ± 13.2	0.1728[1]

Height	cm	x±dp	155.9 ± 10.3	152.4 ± 8.8	154.6 ± 9.4	154.1 ± 9.4	0.6743[1]
BMI	kg/m^2	x±dp	26.9 ± 4.1	26.3 ± 4.5	23.2 ± 3.9	26.0 ± 4.4	0.1129[1]
HGS-bd	Kg	x±dp	16.5 ± 10.1	12.2 ± 7.2	12.8 ± 8.2	13.9 ± 8.6	0.4745[1]
HGS-be	Kg	x±dp	15.6 ± 9.1	11.4 ± 7.2	11.4 ± 7.1	13.0 ± 8.0	0.3847[1]
HGS average	Kg	x±dp	16.0 ± 9.6	11.8 ± 7.1	12.1 ± 7.6	13.4 ± 8.2	0.4618[1]
AC	P10 – P90	n (%)	7 (43.8)	8 (42.1)	4 (50.0)	19 (44.2)	1.0000[3]
	>P90 – P95	n (%)	9 (56.3)	11 (57.9)	4 (50.0)	24 (55.8)	
TSF	P10 – P90	n (%)	8 (50.0)	10 (52.6)	4 (50.0)	22 (51.2	0.9854[2]
	>P90 – P95	n (%)	8 (50.0)	9 (47.4)	4 (50.0)	21 (48.8)	
AMC	P10 – P90	n (%)	9 (56.3)	11 (57.9)	8 (100.0)	28 (65.1)	0.0715[2]
	>P90 – P95	n (%)	7 (43.8)	8 (42.1)	0 (0.0)	15 (34.9)	
SSF	P5 – <P10	n (%)	1 (6.3)	2 (10.5)	0 (0.0)	3 (7.0)	1.0000[3]
	P10 – P90	n (%)	15 (93.8)	17 (89.5)	8 (100.0)	40 (93.0)	
CC (cm)	>31 cm	n (%)	13 (81.3)	14 (73.7)	4 (50.0)	31 (72.1)	0.3240[3]
	≤31 cm	n (%)	3 (18.8)	5 (26.3)	4 (50.0)	12 (27.9)	
WC (cm)	no risk	n (%)	2 (12.5)	4 (21.1)	1 (12.5)	7 (16.3)	0.8653[3]
	with risk	n (%)	14 (87.5)	15 (78.9)	7 (87.5)	36 (83.7)	
IMC (kg/m$^{2)}$)	22 – 27	n (%)	7 (43.8)	9 (47.4)	5 (62.5)	21 (48.8)	0.6600[3]
	<22	n (%)	2 (12.5)	3 (15.8)	2 (25.0)	7 (16.3)	
	>27	n (%)	7 (43.8)	7 (36.8)	1 (12.5)	15 (34.9)	

MNA	eutrophic	n (%)	10 (62.5)	8 (42.1)	1 (12.5)	19 (44.2)	0.0658³
	MR	n (%)	6 (37.5)	11 (57.9)	7 (87.5)	24 (55.8)	
TAPM (mm)	minimum (7 or 5)	n (%)	15 (93.8)	18 (100.0)	7 (87.5)	40 (95.2)	-
	median (12 or 11)	n (%)	1 (6.3)	0 (0.0)	1 (12.5)	2 (4.8)	
	maximum (20 or 18)	-	-	-	-	-	
CLAPA	sedentary	n (%)	9 (56.3)	11 (57.9)	6 (75.0)	26 (60.5)	0.7758³
	active	n (%)	7 (43.8)	8 (42.1)	2 (25.0)	17 (39.5)	

[1] Kruskal-Wallis test; [2] Chi-square test; [3] Fisher's exact test.

Legend:- CDR: clinical dementia rating; BMI: body mass index; HGSra: hand grip strength - right arm; HGSla: hand grip strength-left arm; HGS Max: maximum handgrip strength; AC: arm circumference; TSF: tricipital skin fold; AMC: arm muscle circumference; SSF: subscapular skin fold; CC: calf circumference; WC: waist circumference; MNA: mini nutritional assessment; MR: risk of malnutrition, TAPM: thickness of the adductor pollicis muscle; CLAPA: classified physical activity. P: percentile.

CDR - L: clinical dementia rating - mild; CDR-M: clinical dementia rating - moderate; CDR - G: clinical dementia rating - serious

In the analysis among all the anthropometry parameters and physical activity classified by IPAQ, no significant statistical difference was found in all the variables studied (Table 2). The other anthropometric data were not significantly related to the practice of Physical Activities in AD elderly (Table 2).

Table 2. Descriptive analysis of the variables studied and comparisons with physical activity by the IPAQ classified.

Variables	Classification		PA sedentary N=26	PA active N=17	Total N=43	P-value
Age	years	x±dp	80.1 ± 7.6	81.3 ± 6.2	80.6 ± 7.0	0.7843¹
Weight	Kg	x±dp	61.1 ± 13.7	63.3 ± 12.7	62.0 ± 13.2	0.5594¹
Height	cm	x±dp	153.3 ± 10.5	155.2 ± 7.4	154.1 ± 9.4	0.4486¹
BMI	kg/m²	x±dp	25.9 ± 4.7	26.1 ± 4.0	26.0 ± 4.4	0.8913¹
HGS-bd	Kg	x±dp	14.0 ± 8.5	13.8 ± 9.0	13.9 ± 8.6	0.9702¹
HGS-be	Kg	x±dp	13.0 ± 7.4	12.9 ± 9.0	13.0 ± 8.0	0.8423¹
HGS average	Kg	x±dp	13.5 ± 7.9	13.4 ± 9.0	13.4 ± 8.2	0.8815¹

AC	P10 – P90	n (%)	10 (38.5)	9 (52.9)	19 (44.2)	0.3499[2]
	>P90 – P95	n (%)	16 (61.5)	8 (47.1)	24 (55.8)	
TSF	P10 – P90	n (%)	12 (46.2)	10 (58.8)	22 (51.2)	0.4164[2]
	>P90 – P95	n (%)	14 (53.8)	7 (41.2)	21 (48.8)	
AMC	P10 – P90	n (%)	16 (61.5)	12 (70.6)	28 (65.1)	0.5427[2]
	>P90 – P95	n (%)	10 (38.5)	5 (29.4)	15 (34.9)	
SSF	P5 – <P10	n (%)	1 (3.8)	2 (11.8)	3 (7.0)	0.5523[3]
	P10 – P90	n (%)	25 (96.2)	15 (88.2)	40 (93.0)	
CC (cm)	>31 cm	n (%)	17 (65.4)	14 (82.4)	31 (72.1)	0.3065[3]
	≤31 cm	n (%)	9 (34.6)	3 (17.6)	12 (27.9)	
WC (cm)	no risk	n (%)	4 (15.4)	3 (17.6)	7 (16.3)	1.0000[3]
	with risk	n (%)	22 (84.6)	14 (82.4)	36 (83.7)	
IMC (kg/m$^{2)}$)	22 – 27	n (%)	12 (46.2)	9 (52.9)	21 (48.8)	0.9154[3]
	<22	n (%)	4 (15.4)	3 (17.6)	7 (16.3)	
	>27	n (%)	10 (38.5)	5 (29.4)	15 (34.9)	
MNA	euthrophic	n (%)	9 (34.6)	10 (58.8)	19 (44.2)	0.1181[2]
	MR	n (%)	17 (65.4)	7 (41.2)	24 (55.8)	

[1] Mann-Whitney test, [2] Chi-square test, [3] Fisher's exact test

Legend:- PA: physical activity, BMI: body mass index; HGS-ra: hand grip strength-right arm; HGS-la: hand grip strength-left arm; HGS: handgrip strength; AC: arm circumference; TSF: tricipital skin fold; AMC: muscle circumference of the arm; SSF: subscapular skin fold; CC: calf circumference; WC: waist circumference; P: percentile; MNA: mini nutritional assessment; MR: malnutrition risk.

When investigating the risk factors associated with the CDR score, using univariate and multiple logistic regression analysis, it was found that in the final model, age (p=0.0481; OR=1.097; 95% CI=1.001; 1,202) and the assessment of nutritional status by MNA (p=0.0159; OR=4,815; 95% CI=1,342; 17,282), were the factors that, together, better discriminated the severity of the disease. Each additional year of age increased by 9.7% the chance of CDR score 2 or 3. The patients' nutritional status by MNA, yielded patients classified as malnourished or at risk of malnutrition with a chance of being a score 2 or 3, 4.8 times higher when compared to the nutritional status of normal weight (Table 3).

Table 3. Risk factors associated with the CDR score, investigated by univariate and multiple logistic regression analysis.

Univariated Analysis				
Variable	**Reference**	**P-value**	**OR**	**CI (95%)**
Age		0.0564	1.088	0.998; 1.187
BMI		0.0896	0.888	0.775; 1.018
HGS		0.1504	0.948	0.882; 1.019
AC		0.1355	0.897	0.779; 1.034
AMC		0.3214	0.990	0.970; 1.010
SSF		0.2401	0.946	0.862; 1.038
WC		0.4333	0.980	0.932; 1.031
CC		0.1137	0.870	0.732; 1.034
TAPM		0.4622	0.926	0.754; 1.137
TSF	eutrophy *versus* ER + excess	0.9576	1.031	0.336; 3.158
SSF	Depletion + DPR *versus* eutrophy + excess	0.8051	0.757	0.083; 6.920
AC	eutrophy *versus* ER +excess	0.8405	1.123	0.364; 3.466
CC	eutrophy *versus* malnutrition	0.1344	0.375	0.104; 1.354
AMC	eutrophy *versus* ER +excess	0.0976	2.817	0.827; 9.593
IMC	eutrophy *versus* overweight	0.2427	2.132	0.599; 7.592
	thinness *versus* overweight	0.2469	2.747	0.497; 15.204
WC	no risk *versus* with risk	0.8261	1.185	0.261; 5.386
MNA	MR+D	0.0248	4.006	1.192; 13.464
	MA *versus* eutrophy			
CLAPA	sedentary *versus* active			
Multiple analysis*				
Variable	**Reference**	**P-value**	**OR**	**CI (95%)**
Age		0.0481	1.097	1.001; 1.202
MNA	MR+MA *versus* euthrophy	0.0159	4.815	1.342; 17.282

Legend:- CDR: clinical dementia rating; BMI: body mass index; HGS: handgrip strength; AC: arm circumference; AMC: arm muscle circumference; SSF: subscapular skin fold; DPR: depletion risk; ER: excess risk; WC: waist circumference; CC: calf circumference; TAPM: thickness of the adductor pollicis muscle; TSF: triceps skin fold; MNA: mini nutritional assessment; MAR malnutrition risk; MA: malnourished; CLAPA: classified physical activity.

* multiple model: stepwise process, model accuracy (statistics): c = 0.725.

IV. DISCUSSION

This investigation used several anthropometric parameters to assess the nutritional status of elderly people with AD, and the initial hypothesis of this investigation was to find an association between the different anthropometric parameters used and the disease severity

score (CDR), yet this association was not observed. In the regression models, investigating what the risk factors associated with the severity of the disease would be, only age and MNA remained in the final model. The MNA addresses in its assessment instrument, the indicators of arm and calf circumference, functional capacity, dietary and body weight changes, nutritional problems, disease, elderly people physical evaluation [26]. And, the present study pointed out MNA (risk of malnutrition and malnutrition), as a predictor of the severity of the disease in elderly people with AD. The pathophysiological mechanisms between nutritional status and AD are not yet fully understood. Our data suggest that older age and risk of malnutrition and malnutrition and nutritional imbalance conditions are associated with greater severity of dementia in elderly people with AD. An association between nutritional status and the rate of cognitive and functional decline was also observed in an observational longitudinal study [11], using MNA, CDR and the Mini-Mental State Exam. In the study in question, it was found that a worsening of the CDR, during dementia, was associated with lower MNA scores [11].

Other studies suggest an association between a greater impairment of nutritional status with more advanced AD stages, faster cognitive and functional decline and higher mortality rates [4,8,28].

Unlike the findings found in this investigation, a prospective study recently carried out in Portugal [29] with elderly patients with AD, showed that malnutrition, unintentional weight loss, low weight, low values of calf circumference and muscle circumference of the arm, of handgrip strength and gait speed, were associated with a higher risk of death, regardless of gender, age, marital status, education and cognitive function status[29]. In our study, among the investigated nutritional variables, only malnutrition was associated with AD. And in a Korean study [7] that investigated the nutritional status and clinical risk factors of malnourished patients, the authors observed that dementia was considered an independent predictor for the risk of malnutrition, further suggesting that cortical thinning in the left temporal regions, could be related to nutritional status. Another recent study with female patients with mild cognitive impairment and early-stage Alzheimer's disease, found malnutrition associated with behavioral and psychiatric symptoms of dementia [30].

Other recent findings [31] suggest that malnutrition may be related not only to impaired cognition, but also to the pathology of AD. The authors pointed out that AD biomarkers were associated with the MNA score, waist circumference and BMI, and the associations with the MNA score remained after adjustment for cognitive performance [31].

The present study found no association between the severity of the disease and the HGS. Different data were recently reported in a study with an elderly Japanese population, which showed a greater decline in HGS in the elderly, associated with the late onset of dementia [21].

As limiting factors of this study, it is highlighted that our service is a university hospital, but not a tertiary public health center in Brazil. This study is cross-sectional, with a relatively small sample of cases, although it is a specific population with elderly population with AD, monitored on an outpatient basis. However, we must consider that the hospital and outpatient service, where our study was conducted, is part of a representative clinical and surgical neurology service that includes AD patients care in a large metropolitan region. Thus, the individuals who participated in this study were representative of all those who undergo routine clinical treatment, besides the fact that this population underwent specific screening that allowed diagnostic tracking of the severity of the disease. These points can be considered the strong points of our investigation. Anyway, further investigations with a larger sample size are still need to assess the impact of these findings. We can also suggest that nutritional counseling be offered to those patients who are at risk of malnutrition.

V.   CONCLUSION

The findings in this study allowed us to conclude that age and MNA, discriminate the severity of AD and were considered risk factors for the severity of the disease.

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